MSc in Evidence-Based Health Care

The MSc in Evidence-Based Health Care will position students to integrate the best available research evidence with their clinical expertise and patient values to make better informed decisions in their field of health care.

This is a joint programme between the Nuffield Department of Primary Care Health Sciences and the Department for Continuing Education’s Continuing Professional Development Centre. The Programme works in collaboration with the renowned Centre for Evidence-Based Medicine in Oxford.

This programme has teachers and contributors who are internationally recognised leaders in the field of evidence-based practice and teaching. The flexible structure of the course has been devised to fit with the structure of specialist training and to accommodate student choice.

Watch the following video for more information about the Programme and the student experience:

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Evidence-Based Diagnosis and Screening

Overview

Evaluating and Interpreting the evidence for diagnostic tests

This module will teach students how to critically appraise and apply the best evidence on diagnostic tests. They will learn how to evaluate and interpret the diagnostic accuracy of tests and procedures in different settings. They will also learn how the evidence can inform screening and monitoring programmes.

The last date for receipt of complete applications is 5pm Friday 6th January 2018. Regrettably, late applications cannot be accepted.

The overall aims of this module are to enable students to:

- Understand the different purposes for doing tests, and the appropriate means to evaluate tests for those purposes
- Be able to formulate focused questions for different diagnostic problems
- Be able to describe the optimal study design to carry out clinical research for the investigation of those questions
- Be able to search effectively for papers for different types of diagnostic questions
- Be able to appraise diagnostic accuracy studies
- Have an understanding of reporting standards for diagnostic test studies
- Know how to appraise systematic reviews of diagnostic studies
- Be able to describe different forms of design-related biases in diagnostic studies
- Be able to understand and calculate various measures of diagnostic accuracy, including sensitivity and specificity and positive and negative likelihood ratios
- Understand how information from multiple diagnostic tests can be evaluated simultaneously
- Understand and be able to determine a basic sample size calculation for a simple diagnostic study
- Have an understanding of how to present results of diagnostic test studies visually and graphically
- Understand how results of research studies influence clinical decisions
- Understand how results of diagnostic tests should be communicated to clinicians
- Have an understanding of the adoption of diagnostic test services into clinical practice
- Understand the pitfalls and problems of screening programmes
- Understand the interplay of diagnosis and monitoring in clinical practice
Horizon scanning reports

The horizon scanning reports summarise why the technology is important, provide an overview of the current available evidence and assess whether it could be adopted in the NHS and if so, what the requirements are for the delivery of the technology into practice.

These reports are freely accessible and disseminated to the NIHR Health Technology Assessment Programme (HTA), the National Institute for Health and Clinical Excellence (NICE) and commissioners of health care services to facilitate adoption and identify further research requirements.

We are funded by the National Institute for Health Research (NIHR) and collaborate with the Health Economics Research Centre at Oxford University.

Find out more about our research

The Oxford Diagnostic Horizon Scan Programme identifies new and emerging diagnostic technologies relevant to primary care in the NHS.

46. Point-of-care devices for detecting diabetic polyneuropathy

Read | Download PDF

45. Point-of-care testing for urinary tract infections

Read | Download PDF

44. Point-of-care HbA1c tests: diagnosis of diabetes

Read | Download PDF
• clinical monitoring (such as failure to act upon test results or monitor patients appropriately) – identified as a problem in 31% of preventable deaths
• diagnosis (such as problems with physical examination or failure to seek a specialist opinion) – identified as a problem in 30% of preventable deaths
• drugs or fluid management – identified as a problem in 21% of preventable deaths

Political drive to screen for pre-dementia: not evidence based and ignores the harms of diagnosis

David G Le Couteur \textsuperscript{1} professor of geriatric medicine, \textsuperscript{2} Janny Doust \textsuperscript{1} professor of clinical epidemiology, \textsuperscript{2} Helen Creasey \textsuperscript{3} dementia specialist, \textsuperscript{2} Carol Brayne \textsuperscript{1} professor of public health

\textsuperscript{1}Centre for Education and Research on Ageing, ANZAC Medical Research Institute and the Charles Perkins Centre, University of Sydney and Sydney Research, Concord, NSW, Australia; \textsuperscript{2}Centre for Research in Evidence Based Practice, Bond University, Brisbane, Australia; \textsuperscript{3}Centre for Education and Research on Ageing, Concord RCH Hospital, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK.

Current policy in many countries is aimed at increasing the rates of diagnosis of dementia and cognitive impairment. This policy of drive has been accompanied by research into early detection of dementia, including preclinical identification of underlying neurological changes that might later be associated with dementia.

Evidence to support their use. Little attention has been paid to the fact that standard memory clinics generates stress for patients and their carers, and expands the use of biomarker testing (cerebrospinal fluid measurements of amyloid and tau) and neuroimaging, with associated costs and morbidity.
What is diagnosis?

The process of identifying a disease by its signs, symptoms and results of various diagnostic procedures

Typically someone with abnormal symptoms consults a physician, who will obtain a history of their illness and examine them for signs of diseases.

The physician formulates a hypothesis of likely diagnoses and may or may not order further tests to clarify the diagnosis.
Diagnosis has different meanings in different contexts

**Pathologist:**
Identification of disease in terms of histological or chemical changes

**Bacteriologist:**
Identification of disease in terms of the infective agent
Diagnosis has different meanings in different contexts

**Specialist doctor:**
The focal point of thought in the treatment of a patient. Diagnosis gives a name to the patient’s ailment, the thinking goes backward to decide about pathogenesis, and forward to predict prognosis and choose therapy.

**Family doctor:**
Diagnosis is an assessment of his patient’s physical, psychological, and social condition.

Feinstein A. 1967
Diagnostic strategies and what tests are used for
How do clinicians make diagnoses?

- Patient history...examination...differential diagnosis...final diagnosis
Diagnostic stages & strategies

- Aim: identify types and frequency of diagnostic strategies used in primary care
  - 6 GPs collected and recorded strategies used on 300 patients.

**Stage**
- **Initiation of the diagnosis**
- **Refinement of the diagnostic causes**
- **Defining the final diagnosis**

**Strategies used**
- **Spot diagnoses**
- **Self-labelling**
- **Presenting complaint**
- **Pattern recognition**
- **Restricted Rule Outs**
- **Stepwise refinement**
- **Probabilistic reasoning**
- **Pattern recognition fit**
- **Clinical Prediction Rule**
- **Known Diagnosis**
- **Further tests ordered**
- **Test of treatment**
- **Test of time**
- **No label**

(Diagnostic strategies used in primary care. Heneghan, et al., BMJ 2009. 20;338:b9462009)
What are tests used for?

- Increase certainty about presence/absence of disease
- Disease severity
- Monitor clinical course
- Assess prognosis – risk/stage within diagnosis
- Plan treatment e.g., location
- Stall for time!

"Off hand, I'd say you're suffering from an arrow through your head, but just to play it safe, I'm ordering a bunch of tests."
Roles of new tests

- **Replacement** – new replaces old
  - E.g. CT colonography for barium enema
- **Triage** – new determines need for old
  - E.g. B-natriuretic peptide for echocardiography
- **Add-on** – new combined with old
  - E.g. ECG and myocardial perfusion scan
Critical appraisal of a diagnostic accuracy study
Diagnostic tests: What you need to know

• Validity of a diagnostic study

• Interpret the results
Defining the clinical question: PICO or PIRT

- **Patient/Problem**
  How would I describe a group of patients similar to mine?

- **Index test**
  Which test am I considering?

- **Comparator… or …Reference Standard**
  What is the best reference standard to diagnose the target condition?

- **Outcome….or….Target condition**
  Which condition do I want to rule in or rule out?
Diagnostic Accuracy Studies

- Series of patients
- Index test
- Reference standard
- Compare the results of the index test with the reference standard, blinded
Primary care

Near patient testing for influenza in children in primary care: comparison with laboratory test

Anthony Harnden, Angela Brueggemann, Sasha Shepperd, Judy White, Andrew C Hayward, Maria Zambon, Derrick Crook, David Mant

Influenza is an important cause of acute respiratory illness in young children. Common complications include febrile convulsions, otitis media, bronchiolitis, and croup. In epidemic years attack rates among preschool children often exceed 40%. During these years children with influenza may account for up to 30% of the increase in antibiotic prescribing. Symptoms and signs of influenza in children are not specific and can mimic a range of other common respiratory viral pathogens. One quick way of reaching a precise diagnosis in primary care is to use a near

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<th>RT-PCR test</th>
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<td>Total</td>
<td>61</td>
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Appraising diagnostic studies: 3 easy steps

Are the results valid?
- Appropriate spectrum of patients?
- Does everyone get the reference standard?
- Is there an independent, blind or objective comparison with the reference standard?

What are the results?

Will they help me look after my patients?
Biases in Diagnostic Accuracy Studies...

The Ugly 5....
1. *Appropriate spectrum* of patients?

Ideally, test should be performed on a group of patients in whom it will be applied in the real world clinical setting

**Spectrum bias:**

study uses only highly selected patients…….perhaps those in whom you would really suspect have the diagnosis
Case-control vs consecutive
2. Do all patients have the *reference standard*?

Ideally all patients get the reference standard test

**Verification bias:**

only *some* patients get the reference standard…..probably the ones in whom you really suspect have the disease
Series of patients

Index test

Ref. Std. A

Compare the results of the index test with the reference standard, blinded
Differential Reference Bias

Series of patients

Index test

Ref. Std. A

Ref. Std. B

Blinded cross-classification
Series of patients

Index test

Reference standard..... includes parts of Index test

Blinded cross-classification
3. **Independent, blind or objective comparison with the reference standard?**

Ideally, the reference standard is independent, blind and objective.

**Observer bias:**

test is very subjective, or done by person who knows something about the patient or samples.
Observer Bias

- Series of patients
  - Index test
  - Reference standard
    - Unblinded cross-classification
Effect of biases on results

Lijmer, J. G. et al. JAMA 1999;282:1061-1066
Near patient testing for influenza in children in primary care: comparison with laboratory test

Anthony Harnden, Angela Brueggemann, Sasha Sheperd, Judy White, Andrew C Hayward, Maria Zambon, Derrick Crook, David Mant

Influenza is an important cause of acute respiratory illness in young children. Common complications include febrile convulsions, otitis media, bronchiolitis, and croup. In epidemic years attack rates among preschool children often exceed 40%. During these years children with influenza may account for up to 30% of the increase in antibiotic prescribing. Symptoms and signs of influenza in children are not specific and can mimic a range of other common respiratory viral pathogens. One quick way of reaching a precise diagnosis in primary care is to use a near

Comparison of near patient testing with reverse transcription polymerase chain reaction (RT-PCR) testing for influenza in children

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Participants, methods, and results
From January to March 2001 and October to March 2002 we asked general practitioners in Oxfordshire to identify children with cough and fever who they thought had more than a simple cold. Using a nasal swab we performed a rapid patient test for influenza (QuickVue; Quidel, San Diego, CA). A research nurse did the test, which took 12 minutes.

We collected a nasopharyngeal aspirate from the other nostril and transported the sample to the laboratory within four hours. The laboratory staff were blind to the result of the rapid patient test. After adding phosphate buffered saline to the aspirate we added the emulsified sample to viral lysis buffer before freezing it at −80°C. We used RT-PCR to convert the extracted nucleic acids from RNA to complementary DNA. We performed a multiplex, nested PCR assay, using primer sets specific to influenza A and B, on all the samples. To validate our results we included quantified tissue culture specimens of influenza A and B as positive controls and water as negative control with every batch of samples tested.

A nasal swab and a nasopharyngeal aspirate were taken from 157 children. The children’s median age was 3 years (range 6 months to 12 years), and 100 were boys. We detected influenza by RT-PCR in 61 children.
The Numbers
Appraising diagnostic tests

Are the results valid?
- Appropriate spectrum of patients?
- Does everyone get the reference standard?
- Is there an independent, blind or objective comparison with the gold standard?

What are the results?
- Sensitivity, specificity
- Likelihood ratios
- Positive and Negative Predictive Values

Will they help me look after my patients?
Blood test can predict Alzheimer's, say researchers

By James Gallagher
Health and science reporter, BBC News

A blood test can accurately predict the onset of Alzheimer's disease, according to US researchers.

They showed that testing levels of 10 fats in the blood could predict - with 90% accuracy - the risk of the disease coming on in the next three years.

Their findings, published in Nature Medicine, will now be tested in larger clinical trials.

Experts said the results needed to be confirmed, but such a test would be "a real step forward".

The number of people living with dementia stands at 44 million around the globe and is expected to treble by 2050.
A nasal swab and a nasopharyngeal aspirate were taken from 157 children. The children’s median age was 3 years (range 6 months to 12 years), and 100 were boys. We detected influenza by RT-PCR in 61 children (39%). The near patient test was positive in 27 of these 61 children, giving a sensitivity of 44% (95% confidence interval 32% to 58%) and a specificity of 97% (91% to 99%) (table). The likelihood ratio for a positive test result was 14.2 (4.5 to 44.7) and for a negative result 0.58 (0.46 to 0.72).
### The 2 by 2 table

<table>
<thead>
<tr>
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<th>Disease</th>
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<tbody>
<tr>
<td>Test</td>
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</tr>
<tr>
<td>+</td>
<td>True positives</td>
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<tr>
<td>-</td>
<td>False negatives</td>
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Sensitivity and Specificity
The 2 by 2 table: Sensitivity

<table>
<thead>
<tr>
<th>Disease</th>
<th>Test</th>
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<tbody>
<tr>
<td>+</td>
<td>a</td>
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<tr>
<td>-</td>
<td>c</td>
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Sensitivity = \( \frac{a}{a + c} \)

- **a**: True positives
- **c**: False negatives

Proportion of people **WITH** the disease who have a **positive test result**.

So, a test with 84% sensitivity....means that the test identifies 84 out of 100 people **WITH** the disease.

Sensitivity = \( \frac{84}{100} \)
**The 2 by 2 table: Specificity**

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<td><strong>-</strong></td>
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<td>75</td>
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Proportion of people **WITHOUT** the disease who have a **negative test result**.

So, a test with 75% specificity will be NEGATIVE in 75 out of 100 people **WITHOUT** the disease.

Specificity = \(\frac{d}{b + d}\)

Specificity = \(\frac{75}{100}\)
The Influenza Example

Disease: Lab Test

Test: Rapid Test

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<tr>
<td>+</td>
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Sensitivity = 27/61 = 0.44 (44%)

Specificity = 93/96 = 0.97 (97%)

There were 61 children who did not have influenza... the rapid test was negative in 93 of them.

There were 96 children who had influenza... the rapid test was positive in 27 of them.
A nasal swab and a nasopharyngeal aspirate were taken from 157 children. The children’s median age was 3 years (range 6 months to 12 years), and 100 were boys. We detected influenza by RT-PCR in 61 children (39%). The near patient test was positive in 27 of these 61 children, giving a sensitivity of 44% (95% confidence interval 32% to 58%) and a specificity of 97% (91% to 99%) (table). The likelihood ratio for a positive test result was 14.2 (4.5 to 44.7) and for a negative result 0.58 (0.46 to 0.72).
Predictive Values
Positive and Negative Predictive Value

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<td>True negatives</td>
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**PPV** = Proportion of people with a **positive test** who **have** the disease.

\[
PPV = \frac{a}{a + b}
\]

**NPV** = Proportion of people with a **negative test** who **do not** have the disease.

\[
NPV = \frac{d}{c + d}
\]
The Influenza Example

<table>
<thead>
<tr>
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<th>Test: Rapid Test</th>
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<td>+</td>
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PPV = $\frac{27}{30} = 90\%$

NPV = $\frac{93}{127} = 73\%$
Your father went to his doctor and was told that his test for a disease was positive. He is really worried, and comes to ask you for help!

After doing some reading, you find that for men of his age:
The prevalence of the disease is 30%
The test has a sensitivity of 50% and specificity of 90%

“Tell me what’s the chance I have this disease?”
Disease has a prevalence of 30%. The test has sensitivity of 50% and specificity of 90%.
Disease has a prevalence of 30%.
The test has sensitivity of 50% and specificity of 90%.
Given a positive test, what is the probability your dad has the disease

End
Of 22 people testing positive, 15 have the disease. So, the chance of disease is $\frac{15}{22} = 68\%$.

- Disease +ve: 30 people
- Disease -ve: 70 people
- Sensitivity = 50%
- False positive rate = 10%
- Prevalence of 30\%
- Sensitivity of 50\%
- Specificity of 90\%
Prevalence of 4%, Sensitivity of 50%, Specificity of 90%

11.6 people test positive........ of whom 2 have the disease

Disease +ve

Disease -ve

4

2

9.6

Sensitivity = 50%

False positive rate = 10%

So, chance of disease is 2/11.6 = 17%
Positive and Negative Predictive Value

NOTE

• PPV and NPV are not intrinsic to the test – they also depend on the prevalence!

• NPV and PPV should only be used if the ratio of the number of patients with the disease and the number of patients without the disease is equivalent to the prevalence of the diseases in the studied population

• Use Likelihood Ratio - does not depend on prevalence
Likelihood Ratios
Likelihood ratios

\[ LR = \frac{\text{Probability of clinical finding in patients with disease}}{\text{Probability of same finding in patients without disease}} \]
Likelihood ratios

Positive likelihood ratio (LR+)
How much more likely is a positive test to be found in a person with the disease than in a person without it?

\[
LR+ = \frac{\text{sens}}{(1-\text{spec})}
\]

Negative likelihood ratio (LR-)
How much more likely is a negative test to be found in a person without the disease than in a person with it?

\[
LR- = \frac{(1-\text{sens})}{(\text{spec})}
\]
What do likelihood ratios mean?

- **LR < 0.1**: strong negative test result
- **LR = 1**: no diagnostic value
- **LR > 10**: strong positive test result
Diagnosis of Appendicitis

McBurney’s point

Rovsing’s sign
If palpation of the left lower quadrant of a person's abdomen results in more pain in the right lower quadrant

Psoas sign
Abdominal pain resulting from passively extending the thigh of a patient or asking the patient to actively flex his thigh at the hip

Ashdown’s sign
Pain when driving over speed bumps
For Example

Speed bump test (Ashdown’s sign):
LR+ = 1.4
LR- = 0.1
Beyond Test Accuracy....
Are the results valid?

- Appropriate spectrum of patients?
- Does everyone get the gold standard?
- Is there an independent, blind or objective comparison with the gold standard?

What are the results?

- Sensitivity, specificity
- Likelihood ratios
- Positive and Negative Predictive Values

Will they help me look after my patients?

- Can I do the test in my setting?
- Do results apply to the mix of patients I see?
- Will the result change my management?
- Costs to patient/health service?
**Will the test apply in my setting?**

- Reproducibility of the test and interpretation in my setting
- Do results apply to the mix of patients I see?
- Will the results change my management?
- Impact on outcomes that are important to patients?
- Where does the test fit into the diagnostic strategy?
- Costs to patient/health service?
What about the news story...?
Blood test that can predict Alzheimer's: Elderly could be given early warning

- The simple blood test could give early warning within three years
- The test could speed the search for new drugs that delay or prevent disease
- Experts are pleased, but it could bring health concerns if no cure is found

By FIONA MACRAE SCIENCE CORRESPONDENT

A simple blood test has been developed that gives healthy elderly people precious early warning they may get Alzheimer's within the next three years.

It is hoped the test, the first to predict accurately who will become ill, could speed the search for new drugs that can delay or even prevent the devastating brain disease.

It could eventually lead to widespread screening in middle-age to identify those most at risk and give them greater warning.
Plasma phospholipids identify antecedent memory impairment in older adults

Mark Mapstone¹, Amrita K Cheema²,³, Massimo S Fiandaca⁴,⁵, Xiaogang Zhong⁶, Timothy R Mhyre⁵, Linda H MacArthur⁵, William J Hall⁷, Susan G Fisher⁸,¹⁴, Derick R Peterson⁹, James M Haley¹⁰, Michael D Nazar¹¹, Steven A Rich¹², Dan J Berlau¹³,¹⁴, Carrie B Peltz¹³, Ming T Tan⁶, Claudia H Kawas¹³ & Howard J Federoff⁴,⁵

Sensitivity: 90%
Specificity: 90%

Dementia Prevalence:
1.3% of the entire UK population
7% of the UK population over 65
Dementia has a prevalence of 1%.
The test has sensitivity of 90% and specificity of 90%.
Given a positive test, what is the probability the person has “preclinical” Alzheimer’s?
So, chance of disease is 1/11 = 9%
Over 65 years:
Prevalence of 7%, Sensitivity of 90%, Specificity of 90%

Disease +ve

7

100

Disease -ve

93

Testing +ve

6

15 people test positive........ of whom 6 have the disease

Disease +ve

Sensitivity = 90%

Testing +ve

6

15 people test positive........ of whom 6 have the disease

Disease -ve

False positive rate = 10%

9

So, chance of disease is 6/15 = 40%
Researcher Howard Federoff took blood samples from hundreds of healthy men and women aged 70-plus. During the next five years, some developed Alzheimer’s. Their blood samples were then compared with the samples taken from the people who remained free of the disease. This flagged up a battery of fats that were present in lower amounts in the blood of those who went on to develop memory problems – despite them appearing healthy at the time they gave blood. Dr Federoff then confirmed the finding on a second group.

Writing in the journal Nature Medicine, he said the test can give two to three years’ warning of Alzheimer’s with 90 per cent accuracy. He said it is the first blood test to accurately forecast if an apparently healthy person will succumb to Alzheimer’s. It is also quicker, cheaper and less invasive than other methods such as expensive scans and painful lumbar punctures.

It isn’t entirely clear how the test works but changes in the blood may be a sign of brain cells deteriorating even when people appear healthy.

Dr Simon Ridley, of Alzheimer’s Research UK, said: ‘More work is needed to confirm these findings, but a blood test to identify people at risk of Alzheimer’s would be a real step forward for research.’

Dr Doug Brown, of the Alzheimer’s Society, said: ‘Having such a test would be an interesting development, but it also throws up ethical considerations. If this does develop in the future people must be given a choice about whether they would want to know, and fully understand the implications.’
The 'breakthrough' iPad game that can spot autism in children with 93% accuracy

- Gave 33 children with autism and 45 without iPad games to play
- Games were coded with ability to track finger movements and gestures
- Following the gameplay, the team analyzed data from both groups
- Found children with autism have a greater force of impact than others

By STACY LIBERATORE FOR DAILYMAIL.COM
PUBLISHED: 00:21, 31 August 2016 | UPDATED: 14:58, 31 August 2016

The way children play iPad games could reveal if they have autism, researchers have found.

They found those with the condition used greater force and moved their finger in different ways.

It is hoped the app could lead to earlier diagnosis and treatment.

Scroll down for video
ARE YOU COMING TO BED?

I CAN’T. THIS IS IMPORTANT.

WHAT?

SOMEONE IS WRONG ON THE INTERNET.
What is the ONE thing I need to remember from today?

Are the results valid?

What are the results?

Will they help me look after my patients?

Don’t believe everything you are told, Ask for the Evidence!
Useful books on diagnostics

- Evidence based Physical Diagnosis. Steven McGee. Saunders
- The Diagnostic Process. John Balla. Cambridge Univ. Press
### Useful journal articles on diagnostics
